

wherein

Het is a bicyclic fused ring heteroaromatic group;

g is zero or the integer 1, 2, 3 or 4;

Each R^{16} , which may be the same or different, is an atom or group $-L^3(Alk^2)_tL^4(R^4)_u$,

L^3 and L^4 , which may be the same or different, are each a covalent bond or a linker atom or group -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -N(R⁸)O-, -N(R⁸)N-, -CON(R⁸)-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)-, or -N(R⁸)SO₂N(R⁸)-,

R^8 is a hydrogen atom or an optionally substituted C₁₋₆alkyl group,

t is zero or the integer 1,

u is an integer 1, 2 or 3,

Alk^2 is an aliphatic or heteroaliphatic chain, and

R^4 is a hydrogen or halogen atom or a group selected from an optionally substituted C₁₋₆alkyl or C₃₋₈cycloalkyl group, -OR⁵ (where R⁵ is a hydrogen atom, an optionally substituted C₁₋₆alkyl or C₃₋₈cycloalkyl group), -SR⁵, -NR⁵R⁶ (where R⁶ is as just defined for R⁵ and may be the same or different), -NO₂, -CN, -CO₂R⁵, -SO₃H, -SOR⁵, SO₂R⁵, -SO₃R⁵, -OCO₂R⁵, -CONR⁵R⁶, -OCONR⁵R⁶, -CSNR⁵R⁶, -COR⁵, -OCOR⁵, -N(R⁵)COR⁶, -N(R⁵)CSR⁶, -SO₂N(R⁵)(R⁶), -N(R⁵)SO₂R⁶, N(R⁵)CON(R⁶)(R⁷) (where R⁷ is a hydrogen atom, an optionally substituted C₁₋₆alkyl or C₃₋₈cycloalkyl group), -N(R⁵)CSN(R⁶)(R⁷) or

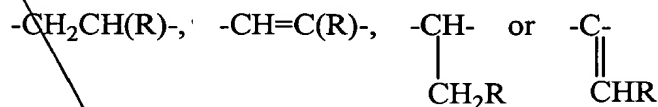
~~-N(R⁵)SO₂N(R⁶)(R⁷),~~

~~provided that when t is zero and each of L³ and L⁴ is a covalent bond then u is the integer 1 and R⁴ is other than a hydrogen atom;~~

~~L² is a covalent bond or an atom or group -O-, -S-, -C(O)-, -C(S)-, -S(O)-, -S(O)₂, -N(R⁸)- or -C(R⁸)(R^{8a})- (where R^{8a} is an atom or group as defined for R⁸ and may be the same or different);~~

~~Ar² is an optionally substituted aromatic or heteroaromatic group;~~

~~Alk is a chain~~



~~in which R is a carboxylic acid (-CO₂H), a carboxylic acid ester, a carboxylic acid amide, or a carboxylic acid biostere;~~

~~R¹ is a hydrogen atom or a C₁₋₆alkyl group;~~

~~L¹ is a covalent bond or a linker atom or group -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -N(R⁸)O-, -N(R⁸)N-, -CON(R⁸)-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)-, or -N(R⁸)SO₂N(R⁸)-;~~

~~Alk¹ is an optionally substituted aliphatic chain;~~

~~n is zero or the integer 1;~~

~~R² is a hydrogen atom or an optionally substituted heteroaliphatic, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkenyl, C₃₋₁₀heterocycloalkyl, C₃₋₁₀heterocycloalkenyl, C₇₋₁₀bicycloalkyl, C₇₋₁₀tricycloalkyl, C₇₋₁₀bicycloalkenyl, C₇₋₁₀tricycloalkenyl, C₇₋₁₀bicycloheteroalkyl, C₇₋₁₀tricycloheteroalkyl, C₇₋₁₀bicycloheteroalkenyl, C₇₋₁₀tricycloheteroalkenyl, aromatic or~~

Sub
B1

A1

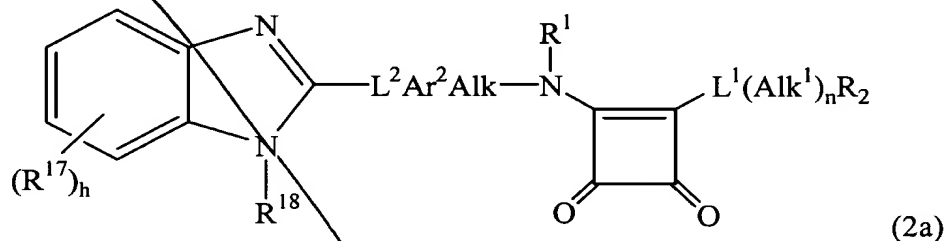
Sub B1
A1
heteroaromatic group, wherein said heteroaliphatic, heterocycloalkyl, heterocycloalkenyl, bicycloheteroalkyl, tricycloheteroalkyl, bicycloheteroalkenyl and tricycloheteroalkenyl groups contain one, two, three, or four heteroatoms or heteroatom-containing groups as defined for L^3 and L^4 , which may be the same or different;

provided that Het is not a 2,6-naphthyridin-1-yl, isoquinolin-1-yl, 2,7-naphthyridin-1-yl or quinazolin-4-yl group;

and the salts, solvates, hydrates and N-oxides thereof.

A2
12. (Amended) A compound according to Claim 1 in which L^1 is a covalent bond, n is zero and R^2 is an optionally substituted C_{5-7} heterocycloalkyl or C_{5-7} heterocycloalkenyl group.

15. (Amended) A compound according to Claim 1 of formula (2a):



wherein:

R^{17} is an atom or group R^{16} as previously defined;

h is zero or the integer 1, 2 or 3;

R^{18} is a hydrogen atom or an atom or group R^{16} as previously defined;

and the salts, solvates, hydrates and N-oxides thereof.

A4
Sub B4
19. (Amended) A compound which is:

~~S-2-[[2-Dipropylamino)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoic acid;~~

~~S-2-[[2-Dipropylamino)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoic acid;~~

~~S-2-[[2-(2-Methylpiperidin-1-yl)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoic acid;~~

~~(S)-3-[4-(Thiophen[2,3-d]pyrimidin-4-ylamino)phenyl]2-(2-(diethylamino-3,4-dioxocyclobut-1-enylamino)propanoic acid;~~

~~and the salts, solvates, hydrates, N-oxides and carboxylic acid esters thereof.~~

~~21. (Amended) A method for the treatment of inflammatory arthritis, multiple sclerosis, allograft rejection, diabetes, inflammatory dermatoses, asthma or inflammatory bowel disease comprising administering to a mammal suffering from such a disease or disorder a therapeutically effective amount of a compound according to Claim 1.~~

~~23. (Amended) A method according to Claim 21 wherein said inflammatory arthritis is selected from the group consisting of rheumatoid arthritis, vasculitis and polydermatomyositis.~~

~~24. (Amended) A method according to Claim 21 wherein said inflammatory dermatoses are selected from the group consisting of psoriasis and dermatitis.~~

~~25. (Amended) A method of inhibiting, in a mammal suffering from a disease or disorder associated with elevated α_4 integrin activity, the binding of α_4 integrins to the ligands~~

thereof, comprising administering to the mammal an effecting amount of a compound according to Claim 1.

26. (Amended) A method according to Claim 25 wherein the α_4 integrins are selected from the group consisting of $\alpha_4\beta_1$ and $\alpha_4\beta_7$ integrins.

Please cancel claim 22, without prejudice.

Please add the following new claim.

27. (New) A compound according to claim 19 wherein the carboxylic acid esters are selected from the group consisting of methyl, ethyl, propyl, and i-propyl.

REMARKS

Following entry of the foregoing amendments, claims 1 to 21 and 23 to 27 will be pending in the application. Claims 1, 12, 15, 19, 21, and 23 to 26 have been amended herein. Claim 22 has been cancelled and new claim 27 has been added, herein.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Preliminarily, Applicants acknowledge with appreciation the Examiner's indication that the compounds defined by the claims are novel in view of the following references: Pamukcu, *et al.*, U.S. Patent No. 6,111,220; Coates, *et al.*, WO 94/29277; and Lombardo, *et al.*, WO 00/35855.